Astrobiology
Lecture 10

From molecular replicators to protocells

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Origin of molecular replication and metabolism

- Conceptual "chicken-egg" problem
  - In present-day cells, nucleic acids and proteins are responsible for replication and metabolic functions, respectively
  - The assemblage of proteins requires the instructions stored in nucleic acids
  - The assemblage of nucleic acids requires the catalytic properties of proteins
  - Each one of these two types of macromolecules requires the previous existence of the other one

- Who came first?
  - Proteins or nucleic acids ?
  - Replication/genetic or metabolic functions ?

Origin of molecular replication and metabolism

- In the past, two opposite schools
  - "Metabolism first"

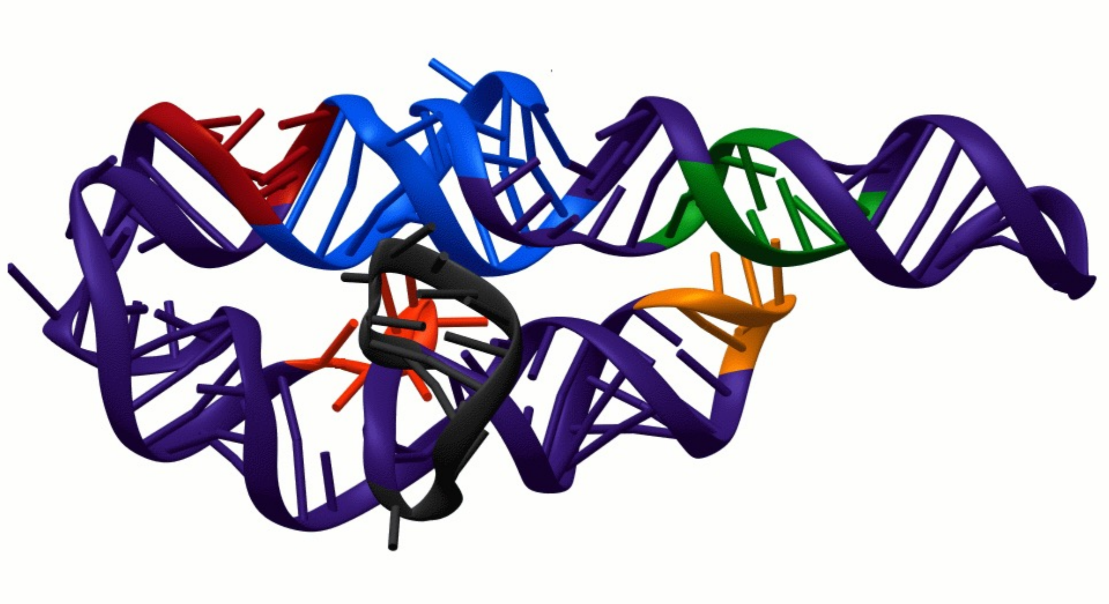
    Emphasizing the initial role of metabolic reactions and the catalytic properties of proteins
  - "Genes first"

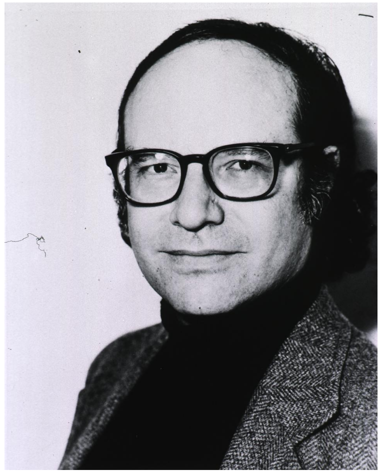
    Emphasizing the initial role of the genetic system and the capability of nucleic acids to store and transmit information

- Present-day approach
  - Appearance of macromolecules that show both genetic and catalytic properties

The "RNA world"

- Present-day, main stream theory in studies on life's origin
- Introduced after the discovery of ribozymes
  - RNA molecules with catalytic properties
- According to this theory, the genetic system is the first to emerge, but with self-catalytic properties
  - Present-day ribozymes would be a sort of molecular fossiles of an ancient "RNA world"





Walter Gilbert

Emergence of the “DNA world”

- Present-day DNA-world would have emerged at a later stage because of its advantages:
  - DNA is more stable
    - The lack of an oxygen atom in the sugar (deoxyribose instead of ribose) makes DNA less reactive than RNA
    - The double DNA strand is more stable than the single RNA strand
    - DNA is better preserved because it is only involved in transcription (not in translation)
    - In eukaryotes DNA is preserved inside the nucleus of the cell
  - The DNA world has an extremely greater flexibility
    - Due to the introduction of proteins specialized in a large variety of metabolic functions

Life as a kinetic state of matter

Addy Pross

Example of the kinetic power of self replication

- Comparison between normal and self-catalytic reactions
  - start with 1 molecule of catalyst *X*
  - assume reaction rate 1μs in both cases
- Time required to build up a mole of products (6 x 10^{23})
  - Normal case: 20 billon years
  - Self-catalytic case: 79 μs
- The kinetic control of chemical reactions could be the key for understanding the origin of life (in chemistry, the term "kinetics" is related to the rate of chemical reactions)
  - see literature by Addy Pross

A, *B*: reactants

X: catalyst

Normal case

$$A + B \xrightarrow{X} C$$

Self-catalytic case

$$A + B \xrightarrow{X} X$$

Replication and molecular evolution

Imperfect replication and chemical selection are supposed to be the key ingredients of some form of <u>molecular evolution</u> that has supposedly led to the molecular machinery that we see today

In a broad sense, *molecular replication and chemical selection is an extension back in time of the concept of Darwinian evolution (reproduction and natural selection)* which, strictly speaking, takes place only after the first living organisms are born

Darwinian evolution, whether of species or molecules, is not teleological

It works *a posteriori*, in the sense that it favours the most suitable variations for a given function that already exists

The capability of replication is probably the key function for the initial selection of biomolecules

Compartments

In order to develop protocells, the early products of the RNA-world must have been enclosed in compartments

Compartmentalization is required to prevent the dispersion of genetic information and to concentrate the action of cooperative biochemical processes in an enclosed space

Membranes delimit a set of structures and reactions that can be transmitted as a specific heritage, paving the road for the onset of Darwinian evolution

Early membranes

In present-day life the compartments are provided by the phospholipid bilayers of the cell membranes

Phospholipds are the result of an evolutionary process, and their synthesis requires enzymatically catalyzed reactions not available for the first protocells

Early membranes could have been constituted by simple fatty acids

Simple fatty acids can be spontaneously generated in prebiotic chemistry, as demonstrated, for example, by their presence in the Murchison meteorite

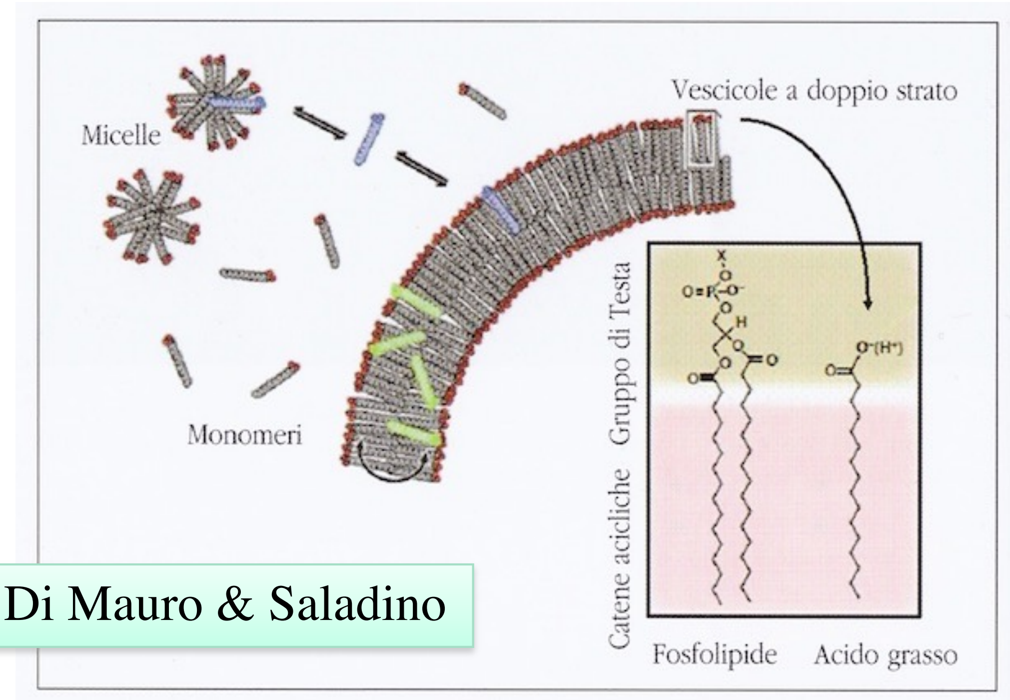


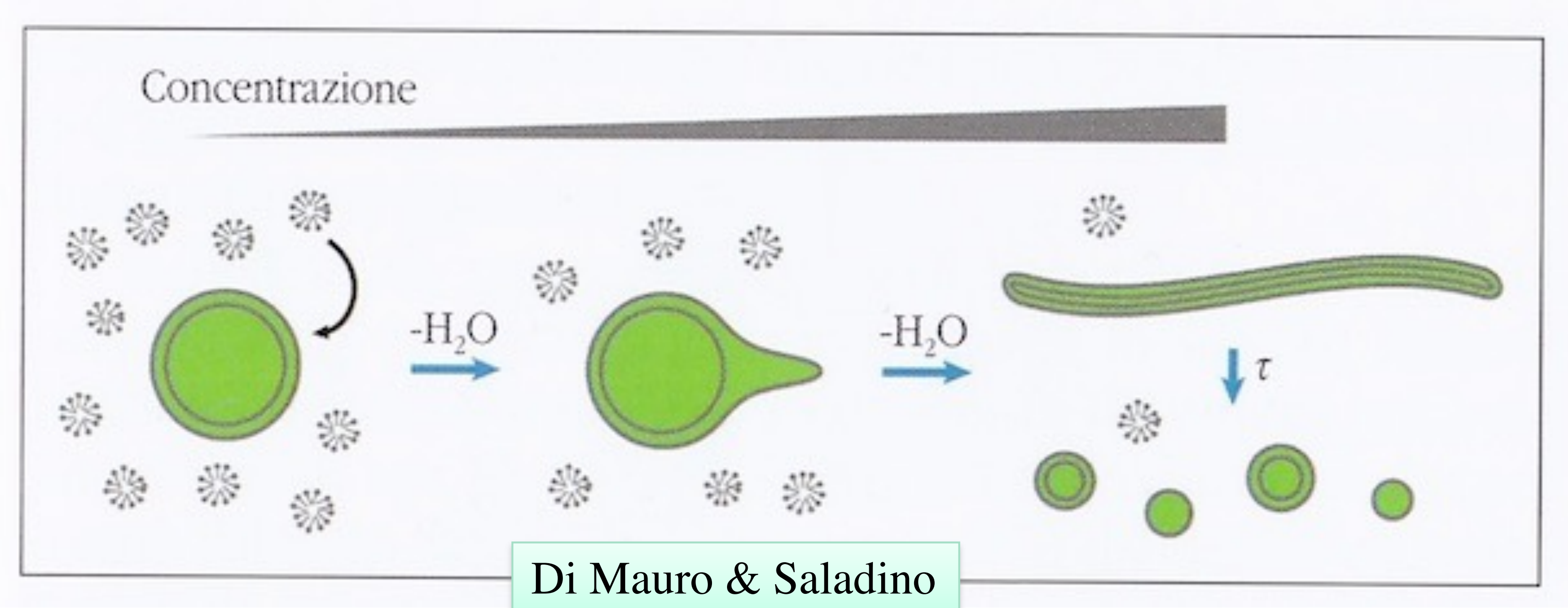
Figure: Di Mauro & Saladino

Protocellular vesicles

Laboratory experiments demonstrate that simple amphiphilic molecules, resulting from prebiotic processes, can give rise to vesicle structures

Variations of the *concentration* of amphiphilic molecules and of *ambient conditions* drive the formation and destruction of vesicle structures that can grow and duplicate

Jack Szostak demonstrated that protocellular vesicles better replicate if they contain RNA and, at the same time, RNA better replicates if it is enclosed in lipidic vesicles



Di Mauro & Saladino

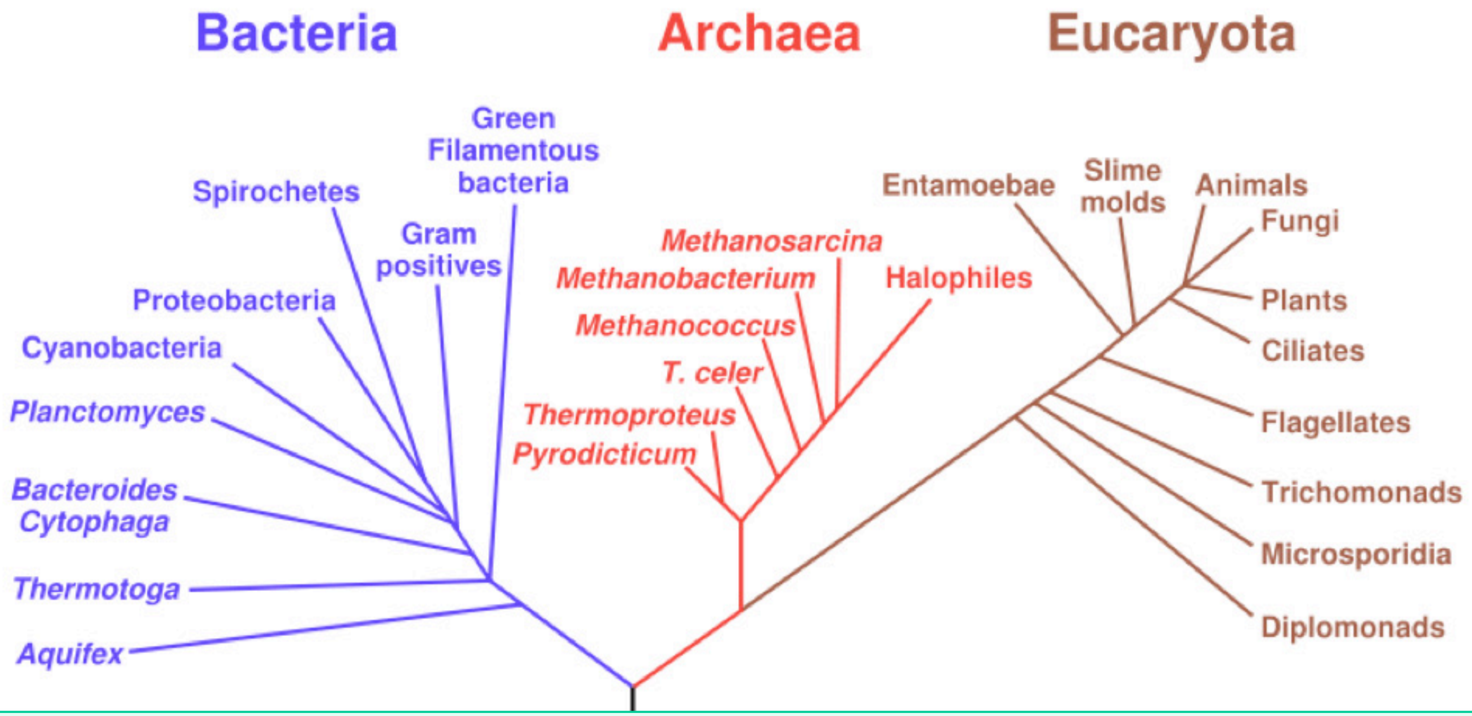
Casting light on the first living cells

- “Top-down” approach
  - From the study of present-day living organisms, we try to characterize the properties of the first terrestrial organisms proceeding backwards in evolution

- The top-down approach is based on the comparison of genetic sequences of different species
  - The techniques of molecular biology allow us to classify species on the basis of their genetic sequences, rather than on their morphology or phenotype

    Phenotype: composite of observable traits and behaviour of organisms
  - The results are visualized in a “phylogenetic tree”, where the distances between different species are proportional to the differences found in the genetic sequences

The phylogenetic tree of life

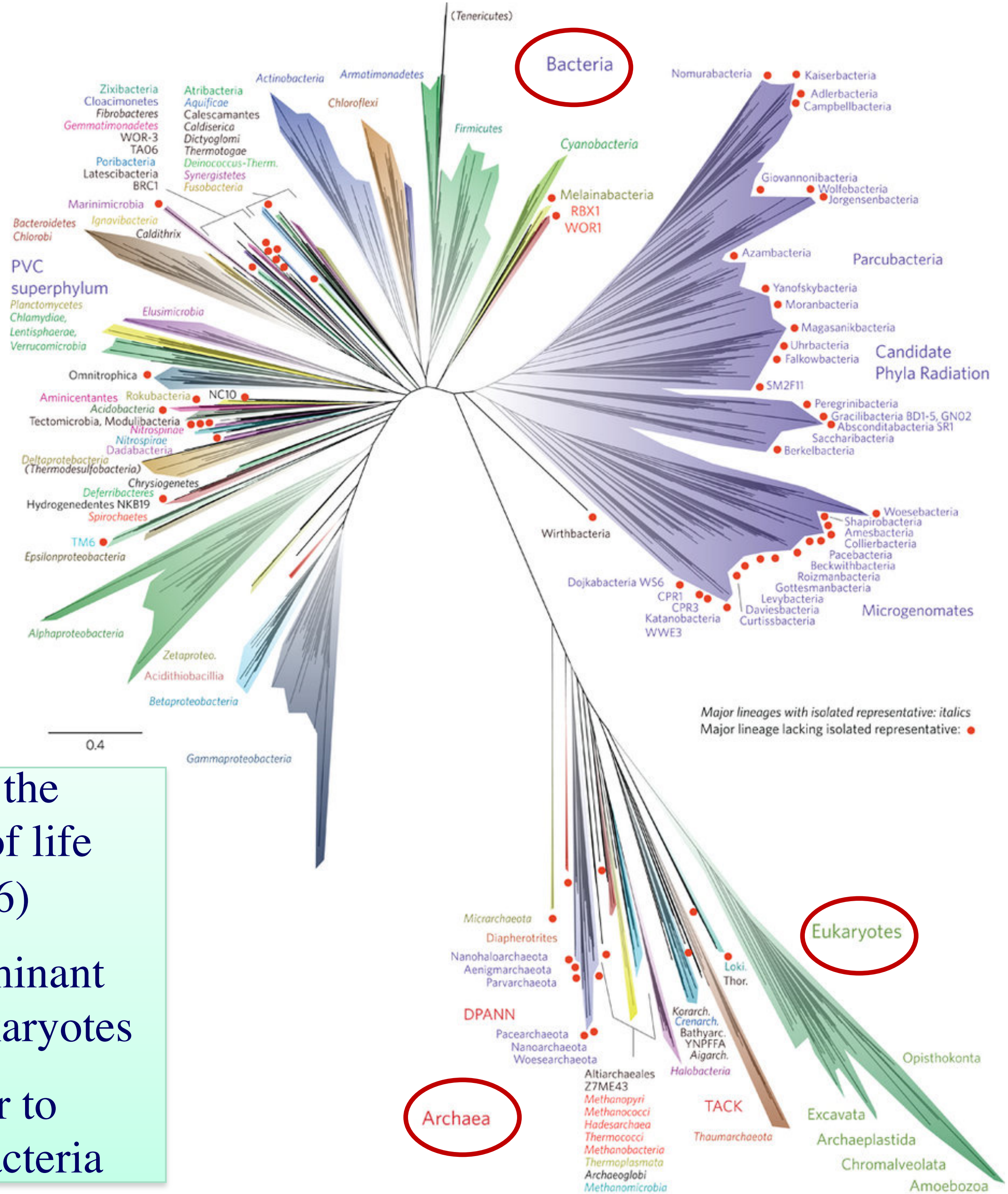


The classification based on genetic sequences has revolutionized our understanding of unicellular organisms

Through genetic classification we have been able to distinguish three domains of unicellular organisms:

Archaea, Eubacteria and Eukaryotes

Archaea were previously classified as bacteria

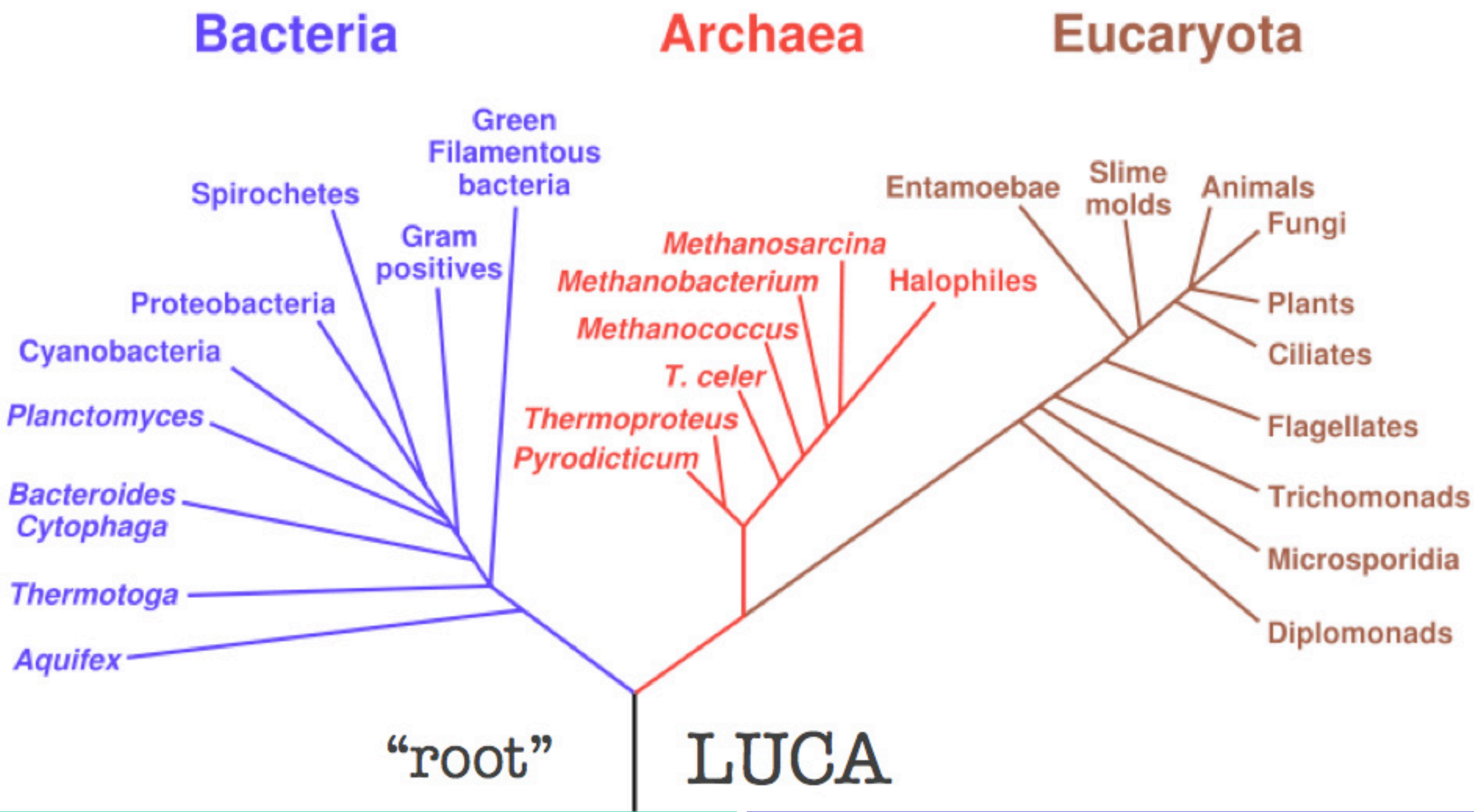


A recent view of the phylogenetic tree of life (Hug et al. 2016)

Bacteria are predominant over archaea and eukaryotes

Archea are closer to Eukaryotes than Bacteria

The Last Universal Common Ancestor

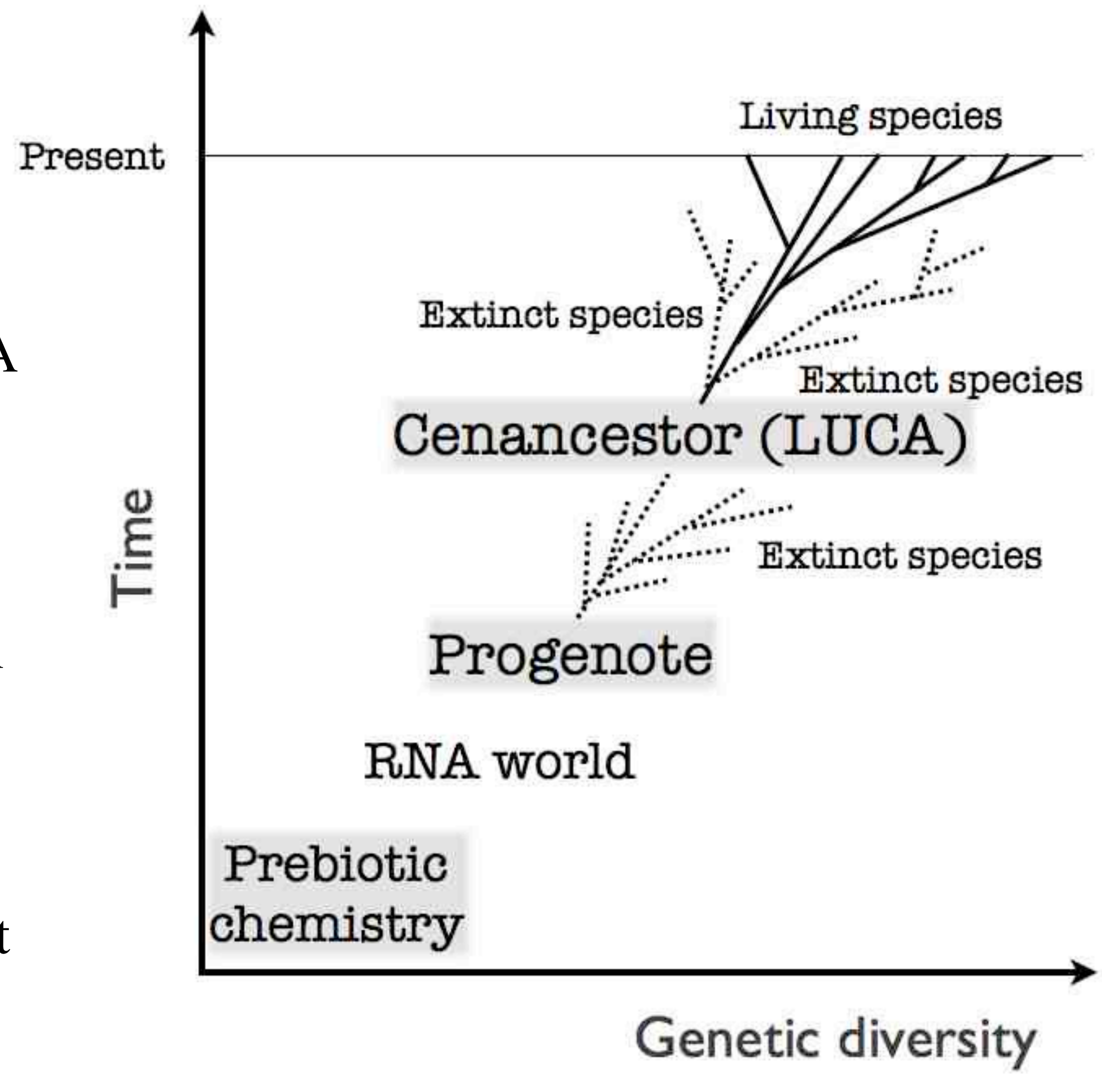


LUCA = Last Universal Common Ancestor of present-day living organisms, also called <u>Cenancestor</u>

Close to the "root" of the tree, we find thermophilic Archaea and Bacteria

The gap between the RNA world and the LUCA

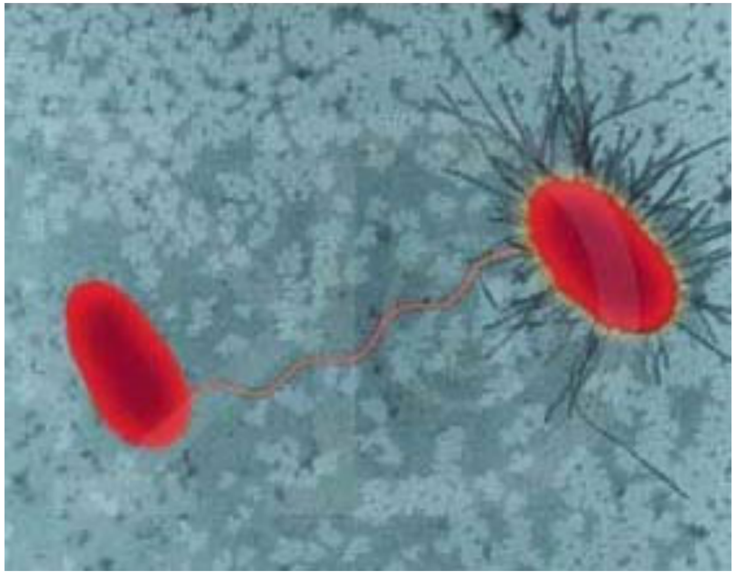
- The root of the phylogenetic tree is not representative of the oldest living cell
  - Other forms of life, extinct in the course of the evolution, must have preceded the LUCA
  - This early form of life is sometimes called the "progenote"
  - The early life could have been a collection of somewhat different cells, rather than a single type of cell
  - Detailed analysis suggests that *early life was mesophilic, rather than thermophilic*

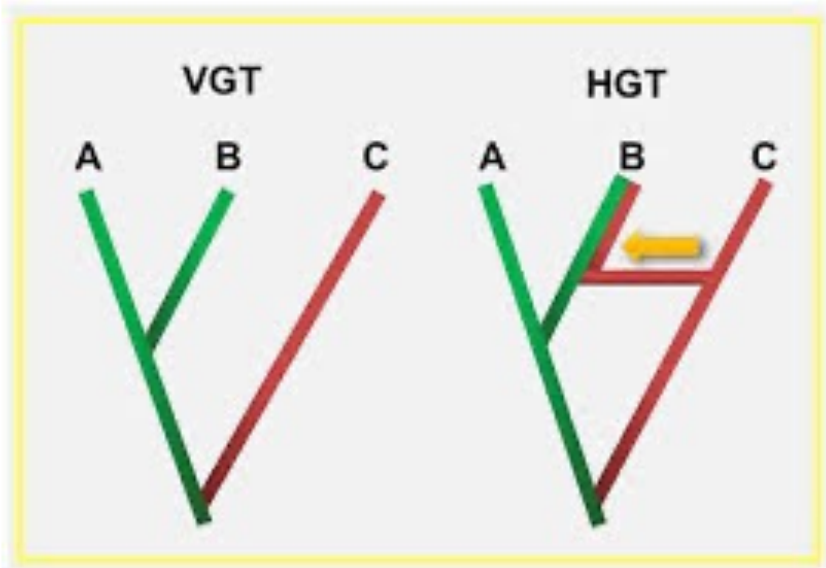


Horizontal gene transfer

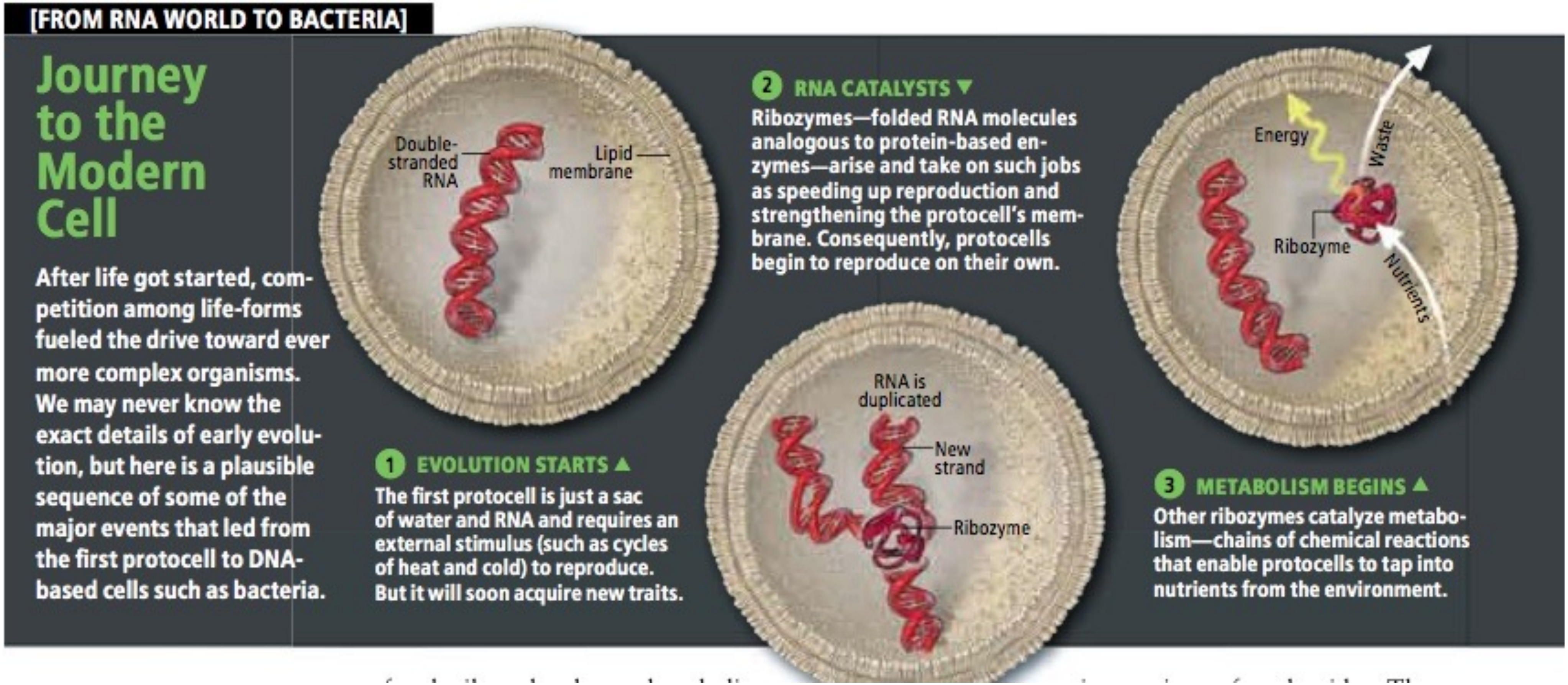
(also called Lateral Gene Transfer)

- Bacteria can exchange genetic material not only during their reproduction ("vertical gene transfer", VGT) but also via direct exchange from one cell to another ("horizontal gene transfer", HGT)
- The existence of HGT complicates the reconstruction of the philogenetic tree, which is based on the VGT scenario
- HGT must have played an essential role in the early stages of life, providing a simple mechanism to exchange genetic material before more complex mechanisms of "vertical" transmission were set in place



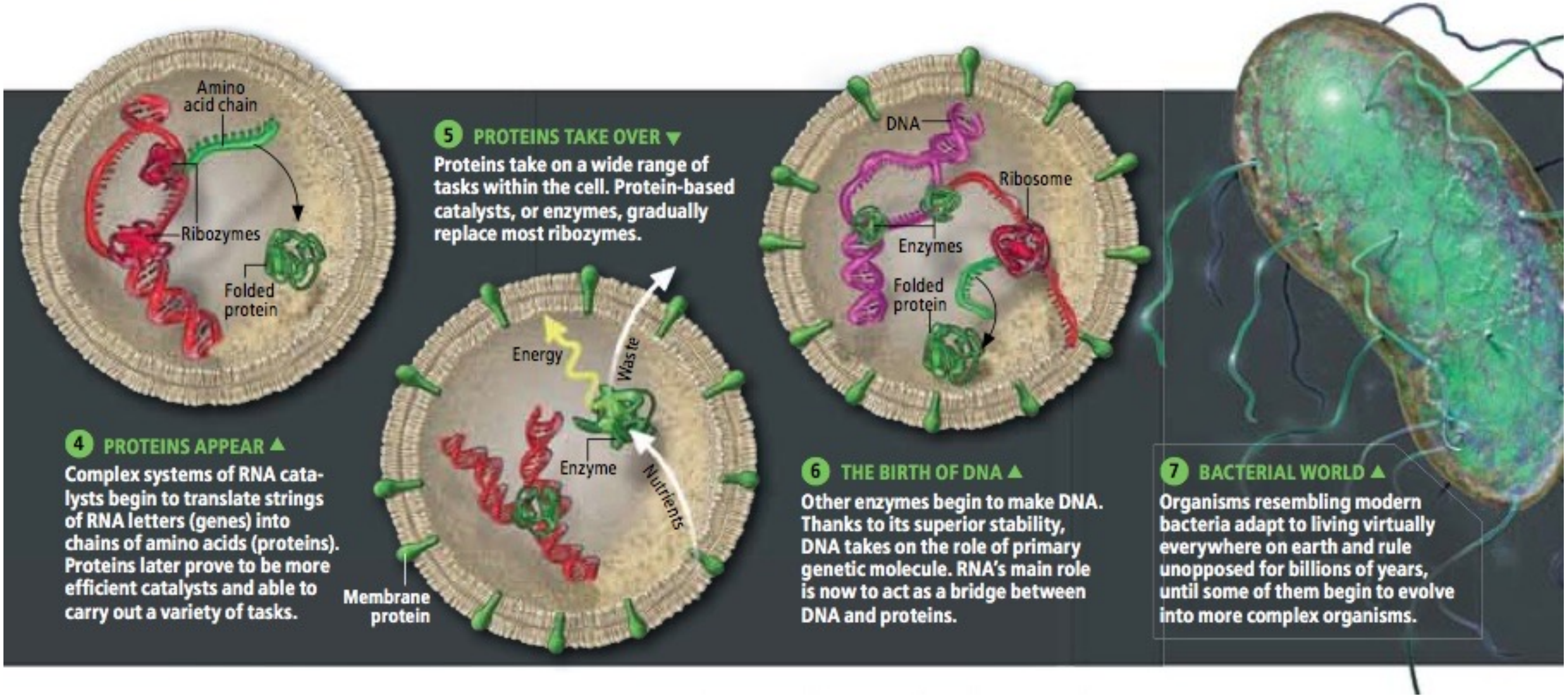


Filling the gap from the RNA world to protocells



Ricardo & Szostak (2009)

Filling the gas from protocells to prokaryotes



Ricardo & Szostak (2009)

The origin of life: autotrophic or heterotrophic?

<u>Autotrophic</u>: the first organisms extract energy and synthesise organic material from the abiotic world

The early life forms would have emerged in the proximity of redox or pH gradients, using the harvested energy to feed biosynthesis reactions.

These processes require extremely reactive chemical environments.

This scenario can only take place in specific thermodynamical niches

<u>Heterotrophic</u>: the first organisms harvest organic material and energy from prebiotic molecules that are already present in the environment

The molecular ingredients could have been synthesized on the primitive Earth and/or could have been delivered on Earth from space

This hypothesis does not require a specific enviromental niche

The cradles of life in the autotrophic scenario

- Deep sea hydrothermal vents
  - An origin of life in the oceans has been often proposed
  - Problems

    Containment of the reactions in an open water environment

    The presence of Na salts would hinder the formation of biological membranes (Natochin 2010)
  - Hydrothermal vents at the bottom of the oceans could provide inorganic compartments, versatile catalysis and sources of organics
  - Advantages: energy flows, chemical gradients

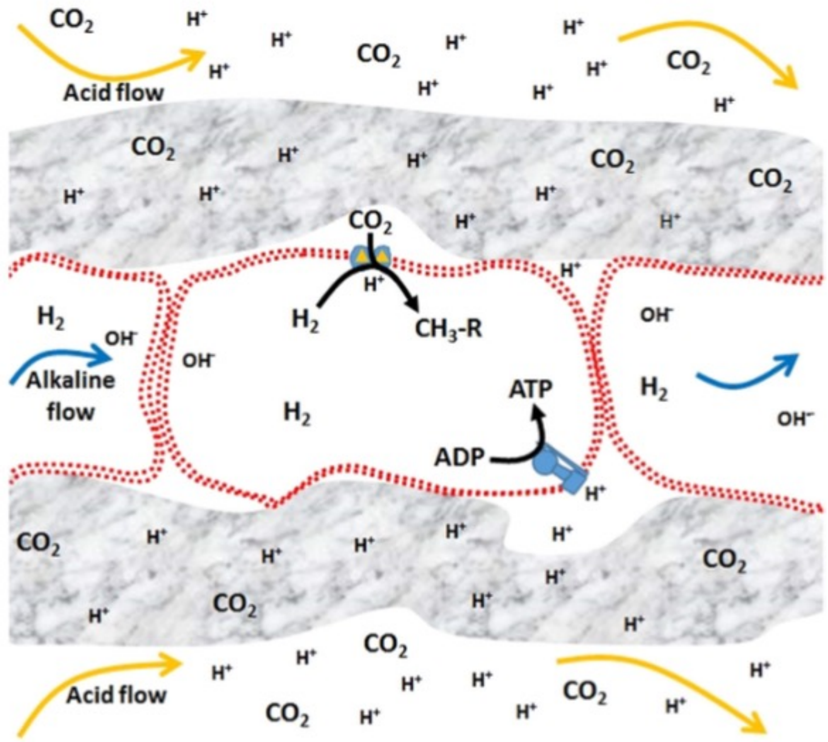


Figure 1. How natural proton gradients could promote CO_2 reduction in organically lined vent pores. A simple leaky protocell within a vent pore, with an Ech and ATP synthase in the lipid membrane, driving both carbon and energy flux, hence, growth and ultimately replication within the vent pores. CH_3-R depicts a methyl group attached to a cofactor and is shorthand for one of the key products of the acetyl CoA pathway, en route to intermediary metabolism.

The cradles of life in the heterotrophic scenario

- Anoxic geothermal fields
  - Geothermal fields are conducive to condensation reactions and enable the involvement of solar light as an energy source and as a selector factor of stable nucleotides
  - Supported by geochemical data and phylogenomic analysis (Mulkidjanian et al. 2012)
  - Geothermal vapour is enriched in phosphorus compounds that could be essential for the emergence of the first RNA-like oligomers

- In the heterotrophic scenarios several different possibilities are considered
  - A Hydrothermal-Sedimentary Context (Westall et al. 2018)